

### Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application.

### Listing of Claims

1. to 46. (cancelled)

47. (currently amended) A method of diagnosing a non-central nervous system (non-CNS) disorder in a subject, the method comprising:

detecting expression of one or more genes in a CNS sample of the subject, wherein the CNS sample ~~is a bodily fluid sample that comprises a protein whose presence or level in the sample is affected by a gene located and expressed in the CNS~~ comprises a cell from the brain of the subject, a cell from the spinal cord of the subject, or cerebrospinal fluid (CSF), and the gene expression data corresponds to the presence or level of the protein in the sample;

generating gene expression data from the detected gene expression;

obtaining a reference gene expression profile for a specific non-CNS disorders; and

comparing the gene expression data with the reference gene expression profile, wherein a match of the CNS sample gene expression data to the reference gene expression profile indicates the subject has or will develop the non-CNS disorder.

48. (currently amended) The method of claim 47, wherein the CNS sample ~~[[is a]]~~ comprises cerebrospinal fluid (CSF) sample, and the gene expression data corresponds to a protein in the CSF.

49. (cancelled)

50. (previously presented) The method of claim 47, wherein the protein is selected from the group consisting of a hormone, a growth factor, an immune system component, and a cytokine.

51. (previously presented) The method of claim 47, wherein the protein is encoded by a gene listed in any of FIGS. 1, 50, and 54, or a human or other mammalian homolog thereof.

52. (previously presented) The method of claim 47, wherein the gene encodes a gene product selected from the group consisting of hepatocyte growth factor (HGF), apherin A3, chemokine (C-C motif) ligand 4, growth differentiation factor-9b (GDF-9b); bone morphogenetic protein 15 (BMP 15), neuroblastoma suppressor of tumorigenicity 1, melanocyte proliferating gene 1, and fibroblast growth factor 22 (FGF 22).

53. (previously presented) The method of claim 47, wherein the CNS sample is a sample of one or more cells from the brain, and the gene expression data corresponds to a nucleic acid molecule or protein in the sample.

54. (previously presented) The method of claim 53, wherein the brain cells are selected from the group consisting of cells from the hypothalamus, the midbrain, the prefrontal cortex, and the striatum.

55. (previously presented) The method of claim 53, wherein the nucleic acid molecule comprises mRNA corresponding to the gene.

56. (previously presented) The method of claim 47, wherein two or more reference gene expression profiles are used, each specific for a different non-CNS disorder.

57. (previously presented) The method of claim 47, wherein the non-CNS disorder is selected from the group consisting of cancer, rheumatoid arthritis, asthma, diabetes, and obesity.

58. (previously presented) The method of claim 47, wherein the non-CNS disorder is cancer.

59. (previously presented) The method of claim 47, wherein the non-CNS disorder is a solid tumor less than 0.5 cm in diameter.

60. (previously presented) The method of claim 47, wherein the gene expression data comprises data for a plurality of genes in the CNS sample, and comprises a gene expression profile.

61. (previously presented) The method of claim 47, further comprising obtaining a control gene expression profile corresponding to one or more healthy subjects; and

comparing the gene expression data with the control gene expression profile, wherein a match of the CNS sample gene expression data to the control gene expression profile indicates the subject does not have and will not likely develop the non-CNS disorder.

62. (previously presented) The method of claim 47, wherein the gene expression is detected using a microarray assay.

63. (previously presented) The method of claim 47, wherein the subject is a human.

64. (previously presented) The method of claim 63, wherein the subject has a family history of the disorder.

65. (previously presented) The method of claim 47, wherein the subject lacks a clinical sign of a disorder as evaluated by imaging analysis.

66. (previously presented) The method of claim 47, wherein the subject is a carrier of a gene associated with an increased risk of developing the disorder.

67. (previously presented) The method of claim 66, wherein the subject is a carrier of the BRCA1, BRCA2, hMSH2, hMLH1, or hMSH6 gene.

68. (previously presented) A method of diagnosing a non-central nervous system (non-CNS) disorder in a subject, the method comprising:

obtaining a test gene expression profile for two or more genes located and expressed in the central nervous system (CNS) of the subject;

obtaining a reference gene expression profile for a specific non-CNS disorder; and

comparing the test gene expression profile with the reference gene expression profile, wherein a test gene expression profile that matches the reference gene expression profile indicates the subject has or will develop the non-CNS disorder.

69. (previously presented) The method of claim 68, further comprising generating a record of the result of the comparing step; and optionally transmitting the record to the subject, health care provider, or other party.

70. (previously presented) The method of claim 68, wherein the non-CNS disorder is selected from the group consisting of cancer, rheumatoid arthritis, asthma, diabetes, and obesity.

71. (previously presented) The method of claim 68, wherein obtaining the test gene expression profile comprises detecting mRNA corresponding to the two or more genes.

72. (previously presented) The method of claim 68, wherein obtaining the test gene expression profile comprises detecting polypeptide products encoded by the two or more genes.

73. (previously presented) The method of claim 68, wherein test gene expression profiles are obtained for a plurality of genes located and expressed in the CNS.

74. (previously presented) The method of claim 68, wherein obtaining the test gene expression profile comprises performing a microarray assay.

75. (previously presented) A method of identifying a disease surveillance gene for a non-central nervous system (non-CNS) disorder in a human, the method comprising:  
inducing a non-CNS disorder in a test experimental animal;  
comparing expression of a gene located in the CNS of the test experimental animal to expression of the gene located in the CNS of a control experimental animal; and  
selecting as a disease surveillance gene a human homolog of a gene that is differentially expressed in the CNS of the test experimental animal compared to the gene expressed in the CNS of the control experimental animal.

76. (previously presented) The method of claim 75, wherein the non-CNS disorder is a neoplasm induced by chemical or radiation mutagenesis.

77. (previously presented) The method of claim 75, wherein the non-CNS disorder is a neoplasm induced by administering a neoplastic cell to the experimental animal.

78. (previously presented) The method of claim 75, wherein the experimental animal is an animal model of rheumatoid arthritis, diabetes, asthma, obesity, or diabetes.

79. (previously presented) The method of claim 75, wherein the experimental animal is a mouse or non-human primate.

80. (previously presented) A reference gene expression profile corresponding to the presence of a non-central nervous system (non-CNS) disorder in a mammal, comprising expression data of 5 or more genes, wherein each of the 5 or more genes is located and differentially expressed in a central nervous system (CNS) of a mammal having a specific non-CNS disorder compared to the same 5 or more genes in a mammal not having the specific non-CNS disorder.

81. (previously presented) The reference gene expression profile of claim 80, wherein the reference gene expression profile comprises expression data of 5 or more genes selected from

any genes listed in one or more of FIGs. 29-1 to 29-6; 32-1 to 32-6; or 35-1 to 35-6 for breast cancer; FIGs. 30-1 to 30-6; 33-1 to 33-6; or 36-1 to 36-6 for colon cancer; FIGs. 31-1 to 31-6; 34-1 to 34-6; or 37-1 to 37-6 for lung cancer; FIG. 50 for arthritis; or FIG. 54 for asthma.

82. (previously presented) The reference gene expression profile of claim 80, wherein the 5 or more genes are selected from any one of the following groups of genes:

Breast Cancer: Nedd8 (FIG. 29-1), Col4a3bp (FIG. 29-2), Bgn (FIG. 29-4), Sox5 (FIG. 29-5), Slc38a4 (FIG. 32-1), Tom1 (FIG. 32-2), Calr (FIG. 32-4), Itgae (FIG. 32-5), Ttrap (FIG. 35-1), Pex11b (FIG. 35-2), Sema7a (FIG. 35-4), and Stam2 (FIG. 35-5);

Colon Cancer: Nmb (FIG. 30-1), Ryr2 (FIG. 30-2), Trfr (FIG. 30-4), Mfap5 (FIG. 30-5), Prrg2 (FIG. 33-1), Faim (FIG. 33-2), Mgrn1 (FIG. 33-4), Stch (FIG. 33-5), Lhb (FIG. 36-1), Prm3 (FIG. 36-2), Crry (FIG. 36-4), and Timp4 (FIG. 36-5);

Lung cancer: Nmb (FIG. 31-1), Pcdh8 (FIG. 31-2), Rock2 (FIG. 31-4), Angptl3 (FIG. 31-5), Sqstm1 (FIG. 34-1), Kcnip2 (FIG. 34-2), Oxt (FIG. 34-4), Myh4 (FIG. 34-5), Enc1 (FIG. 37-1), Gsg1 (FIG. 37-2), Srr (FIG. 37-4), and Ndph (FIG. 37-5);

Arthritis: Bcl2l1 (FIG. 51A), P2rx1 (FIG. 51B), Pafah1b1 (FIG. 51B), Kcna3 (FIG. 51C), Taf1b (FIG. 51C), Slc38a3 (FIG. 51D), Hprt (FIG. 52A), C1d (FIG. 52B), Car11 (FIG. 52D), Dusp3 (FIG. 52D), Gabrr2 (FIG. 53C), and Aatk (FIG. 53D); and

Asthma: Rasa3 (FIG. 55B), Tnk2 (FIG. 55B), H28 (FIG. 55C), Diap2 (FIG. 55C), Lgals6 (FIG. 56A), Reck (FIG. 56A), Whrn (FIG. 56A), Stk22s1 (FIG. 56B), CD47 (FIG. 57A), Jund1 (FIG. 57A), Cstb (FIG. 57B), and Desrt (FIG. 57B).

83. (previously presented) A computer-readable medium comprising a data set corresponding to a reference gene expression profile of claim 80.

84. (previously presented) A method of generating a reference gene expression profile of claim 80, the method comprising:

- obtaining a control mammal not having the specific non-CNS disorder;
- obtaining a diseased mammal of the same type as the control mammal that has the specific non-CNS disorder;

generating a first gene expression profile from the one or more genes located and expressed in the CNS of the control mammal and a second genetic expression profile from the one or more genes located and expressed in the CNS of the diseased mammal;

comparing the first and second genetic expression profiles;

selecting a set of genes from the second genetic expression profile that are differentially expressed; and

preparing the reference gene expression profile from expression data from the selected genes.

85. (cancelled) A system for diagnosing a non-central nervous system (non-CNS) disorder in a subject, the system comprising:

a sampling device to obtain a central nervous system (CNS) sample;

a gene expression detection device that generates gene expression data for one or more genes in the CNS sample or an imaging device to obtain an image of gene expression of one or more genes in the CNS and generate gene expression data for the one or more genes;

a reference gene expression profile of claim 80 for a specific non-CNS disorder; and

a comparator that receives and compares the gene expression data with the reference gene expression profile.

86. (new) The method of claim 47, wherein the gene encodes a gene product selected from the group consisting of:

For Breast Cancer: Nedd8 (FIG. 29-1), Col4a3bp (FIG. 29-2), Bgn (FIG. 29-4), Sox5 (FIG. 29-5), Slc38a4 (FIG. 32-1), Tom1 (FIG. 32-2), Calr (FIG. 32-4), Itgae (FIG. 32-5), Ttrap (FIG. 35-1), Pex11b (FIG. 35-2), Sema7a (FIG. 35-4), and Stam2 (FIG. 35-5);

For Colon Cancer: Nmb (FIG. 30-1), Ryr2 (FIG. 30-2), Trfr (FIG. 30-4), Mfap5 (FIG. 30-5), Prg2 (FIG. 33-1), Faim (FIG. 33-2), Mgm1 (FIG. 33-4), Stich (FIG. 33-5), Lhb (FIG. 36-1), Prm3 (FIG. 36-2), Crry (FIG. 36-4), and Timp4 (FIG. 36-5);

For Lung cancer: Nmb (FIG. 31-1), Pcdh8 (FIG. 31-2), Rock2 (FIG. 31-4), Angptl3 (FIG. 31-5), Sqstm1 (FIG. 34-1), Kcnip2 (FIG. 34-2), Oxt (FIG. 34-4), Myh4 (FIG. 34-5), Enc1 (FIG. 37-1), Gsg1 (FIG. 37-2), Srr (FIG. 37-4), and Ndph (FIG. 37-5);

For Arthritis: Bcl2l (FIG. 51A), P2rx1 (FIG. 51B), Pafah1b1 (FIG. 51B), Kcna3 (FIG. 51C), Taf1b (FIG. 51C), Slc38a3 (FIG. 51D), Hprr (FIG. 52A), C1d (FIG. 52B), Car11 (FIG. 52D), Dusp3 (FIG. 52D), Gabrr2 (FIG. 53C), and Aatk (FIG. 53D); and

For Asthma: Rasa3 (FIG. 55B), Tnk2 (FIG. 55B), H28 (FIG. 55C), Diap2 (FIG. 55C), Lgals6 (FIG. 56A), Reck (FIG. 56A), Whrn (FIG. 56A), Stk22s1 (FIG. 56B), CD47 (FIG. 57A), Jund1 (FIG. 57A), Cstb (FIG. 57B), and Desrt (FIG. 57B).